UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,722	04/23/2001	Michael C. MacLeod	UTSC:607USC1	5071

7590 01/26/2005

David L. Parker
FULBRIGHT & JAWORSKI, L.L.P.
Suite 2400
600 Congress Avenue
Austin, TX 78701

EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,722	MACLEOD ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,20,21,23-29,36-76 and 85-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,20,21,23-29,36-76 and 85-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 April 2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Appeal Brief

1. In view of the appeal brief filed on November 8, 2004 and newly found rejections summarized herein, **PROSECUTION IS HEREBY REOPENED**. New ground of rejection are set forth below. The claims pending in this application are claims 3, 4, 20, 21, 23-29, 36-76 and 85-89. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn.

To avoid abandonment of the application, applicant must exercise one of the following two options:

file a replay under 37 CFR 1.111; or request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1,131, or 1.132) or other evidence are permitted. See 37 CFR 1.93 (b) (2).

Priority

2. Since this instant application is a continuation of case 09/414,847, now US Patent No. 6,221,600. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Objections

3. Claim 20 is objected to because of the following informalities: (1) "said primer" in i) of step b) should be 'said first primer"; and (2) "said primer" in ii) of step b) should be 'said second primer".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3, 4, 20, 21, 23-29, 36-76 and 85-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To the extent that the claimed composition/or methods are not described in the instant disclosure, claims 3, 4, 20, 21, 23-29, 36-76 and 85-89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

The specification fails to define or provide any disclosure to support the phrases "a predetermined 5' sequence" and "a predetermined linker" in claims 87 and 88 and two random primers recited in claim 20. The specification only teaches RT-PCR using a random hexamer (see page 9, lines 15-20).

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 87-89 are rejected under 35 U.S.C. 102(e) as being anticipated by Senapathy (US Patent No. 5,994,058, filed on March 20, 1995).

Regarding claim 87, Senapathy teaches a primer molecule with a 3' terminal specificity region of from 3-8 nucleotides in length, the specificity region defined as one of all possible sequence combinations A,T,G or C (see primer A in Figure 1 and column 3). Since a pair of primer molecules or a population of paired primer molecules can be identical and 5' end of the primer A taught by Senapathy has an ability to anneal to a linker sequence, Senapathy discloses a pair of primer molecules (ie., two identical primer A) wherein both members of the pair comprise (a) a predetermined 5' sequence that incorporates a sequence that anneals to 5' predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the specificity region defined as one of all possible sequence combinations of A, T, G and C as recited in claim 87, a population of paired primer molecules (ie., multiple identical primer A), the primer molecule pairs having (a) a predetermined 5' sequence that incorporates a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C as recited in claim 88 wherein a primer molecule pair selected from the population of claim 88 as recited in claim 89.

Therefore, Senapathy teaches all limitations recited in claims 87-89.

Response to Arguments

In page 4 , second paragraph bridging to page 5, third paragraph of the appeal brief filed on November 8, 2004, applicant argues that: (1) Senapathy does not teach "primer pairs wherein both members of the pairs incorporate random sequences in their specificity regions"; (2) Senapathy does not teach incorporates a sequence that anneals to a predetermined linker

sequence; and (3) "the Examiner must demonstrate prior art that actually shows a primer that incorporates a sequence that binds to a linker. This has not been done. In any event, the claims now refer to a primer pair, wherein each member of the pair incorporates a sequence that binds to a *different* linker sequence, and are thus still further removed from the prior art".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, since a pair of primer molecules or a population of paired primer molecules can be identical and Senapathy teaches a primer molecule with a 3' terminal specificity region of from 3-8 nucleotides in length, the specificity region defined as one of all possible sequence combinations A,T,G or C (see primer A in Figure 1 and column 3), Senapathy does teach primer pairs (ie., two identical primer A) wherein both members of the pairs incorporate random sequences in their specificity regions. Second, since the phrase "that incorporates a sequence that anneals to 5' predetermined linker sequence" recited in claims 87 and 88 are functional language of the claims and 5' end of the primer A taught by Senapathy has an ability to anneal to a linker sequence, Senapathy discloses a predetermined 5' sequence that incorporates a sequence that anneals to 5' predetermined linker. Third, claims 87-89 do not require that each member of the pair incorporates a sequence that binds to a different linker sequence as suggested by applicant.

8. Claims 87-89 are rejected under 35 U.S.C. 102(b) as being anticipated by Sliver *et al.*, (US Patent No. 5,104,792, published on April 14, 1992).

Regarding claims 87-89, Sliver *et al.*, teach a primer molecule with a 3' terminal specificity region of from 3-8 nucleotides in length, the specificity region defined as one of all

possible sequence combinations A,T,G or C (see universal primer in Figure 1 and column 2). Since a pair of primer molecules or a population of paired primer molecules can be identical and 5' end of the universal primer taught by Sliver *et al.*, has an ability to anneal to a linker sequence, Sliver *et al.*, disclose a pair of primer molecules (ie., two identical universal primers) wherein both members of the pair comprise (a) a predetermined 5' sequence that incorporates a sequence that anneals to 5' predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the specificity region defined as one of all possible sequence combinations of A, T, G and C as recited in claim 87, a population of paired primer molecules (ie., multiple identical universal primers), the primer molecule pairs having (a) a predetermined 5' sequence that incorporates a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C as recited in claim 88 wherein a primer molecule pair selected from the population of claim 88 as recited in claim 89.

Therefore, Sliver *et al.*, teaches all limitations recited in claims 87-89.

Response to Arguments

In page 6, second paragraph bridging to page 7, second paragraph of the appeal brief filed on November 8, 2004, applicant argues that: (1) "the primers of Silver that contain random specificity regions are shown ***not*** to have 5' region that bind their template"; and (2) Sliver *et al.*, do not teach a linker.

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, since 5' end of the universal primer taught by Sliver *et al.*, has

an ability to anneal to a linker sequence, the primers of Silver *et al.*, that contain random specificity regions have 5' region that incorporates a sequence that anneals to 5' predetermined linker sequence. Second, there is no phrase "their template" as suggested by applicant. Third, a linker is not structural limitation of the primers recited in claims 87-89.

9. Claims 87-89 are rejected under 35 U.S.C. 102(e) as being anticipated by Senapathy (US Patent No. 6,521,428 B1, priority date: April 21, 1999).

Regarding claims 87-89, since Senapathy teaches a plurality of first primers wherein each first primer comprising (i) a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long and (ii) a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3' to the region of fixed nucleotide sequence and a plurality of second primers wherein each second primer comprising (i) a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long and (ii) a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3 ' to the region of fixed nucleotide sequence (see claim 25 in column 26) and 5' end of each of the first and second primers taught by Senapathy has ability to anneal to a linker sequence, Senapathy discloses a pair of primer molecules (ie., one first primer and a second primer) wherein both members of the pair comprise (a) a predetermined 5' sequence that incorporates a sequence that anneals to 5' predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the specificity region defined as one of all possible sequence combinations of A, T, G and C as recited in claim 87, a population of paired primer molecules (ie., a plurality of first and second primers), the

primer molecule pairs having (a) a predetermined 5' sequence that incorporates a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C as recited in claim 88 wherein a primer molecule pair selected from the population of claim 88 as recited in claim 89.

Therefore, Senapathy teaches all limitations recited in claims 87-89.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 3, 4, 20, 23, 27-29, 36-42, 45, 46, 61-75, 85 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Senapathy (April 21, 1999) as applied to claims 87-89

above, and further in view of Issaacs *et al.*, (US Patent No. 5,139,940, published on April 18, 1992).

Regarding claim 1, since Senapathy teaches a method for amplifying a nucleic acid template comprising: (a) providing a plurality of first primers, each first primer comprising (i) a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long and (ii) a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3' to the region of fixed nucleotide sequence; (b) providing a plurality of second primers, each second primer comprising (i) a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long and (ii) a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3 ' to the region of fixed nucleotide sequence, wherein the regions of fixed nucleotide sequence in the second plurality of primers is shorter than the regions of fixed nucleotide sequence in the first plurality of primers; and (c) amplifying a first region of the nucleic acid template with the plurality of first primers and the plurality of second primers, wherein at least one primer from within each of the plurality of first primers and the plurality of second primers anneals specifically to the template (see Figures 4 and 5, and claim 25 in column 26), Senapathy discloses obtaining a DNA molecule having a first linker sequence positioned at one end of the DNA molecule (ie., 5' of the nucleic acid template taught by Senapathy) and a second linker sequence (ie., 3' of the nucleic acid template taught by Senapathy), different from said first linker sequence, positioned at the other end of the DNA molecule, and subjecting said DNA to a DNA synthesis reaction with a primer set comprising: i) a first primer, wherein the 3' sequence of said first primer comprises a specificity region, and a second primer, wherein the 3'

sequence of said second primer comprises a specificity region wherein both the specificity regions of both the first and second primers comprise random sequences as recited in claim 20.

Regarding 3 and 4, Senapathy teaches that said DNA is non-genomic DNA and said DNA is cDNA (see column 5, first paragraph).

Regarding claims 23, 85 and 86, Senapathy teaches that the first and second primers are employed to amplify the DNA molecule and the first and second primers are employed to sequence the DNA molecule, and further comprising identifying the amplified DNA (see column 19).

Regarding claims 27-29, Senapathy teaches that the specificity region of the primers of the first primer set is 3,4,5,6,7 or 8 base pairs long and the specificity region of the primers of the second primer set is 3,4,5,6,7 or 8 base pairs long, and said amplification comprises polymerase chain reaction.

Regarding claims 36-38, Senapathy teaches that a label is incorporated into said amplified DNA wherein said label is incorporated by means of a labeled primer and further comprising partial nucleotide sequence identification of the amplified products by the identity of the label (see column 19).

Regarding claim 39-42, Senapathy teaches that said label is a chromophore wherein said label is an affinity label or said label is a fluorophore or said label is a dye.

Regarding claims 45 and 46, Senapathy teaches that the products of said DNA synthesis reaction is analyzed as recited in claim 45 (see column 19). Since Senapathy teaches sequencing the PCR products and it is known that DNA sequencing is performed by polyacrylamide gel

electrophoresis; Senapathy teaches that said analysis of products is by polyacrylamide gel electrophoresis as recited in claim 46.

Regarding claims 61-76, since the method taught by Senapathy can be used in any kind of template, it is obvious to use the method taught by Senapathy in DNA recited in claims 61-76.

Senapathy does not disclose that the 5' sequence of said first primer is complementary to said first linker sequence and the 5' sequence of said second primer is complementary to said second linker sequence as recited in step b) of claim 20.

Issaacs *et al.*, teach to amplify a double stranded DNA using a first and a second primer wherein 5' sequence of said first primer is complementary to 5' of one strand of the double stranded DNA and the 5' sequence of said second primer is complementary to 5' of another strand of the double stranded DNA (see Figure 36).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 20 using a first and a second primer wherein 5' sequence of said first primer is complementary to said first linker sequence and the 5' sequence of said second primer is complementary to said second linker sequence in view of the patents of Senapathy and Issaacs *et al.*. One having ordinary skill in the art would have been motivated to do so because Issaacs *et al.*, has successfully amplified a double stranded DNA using a first and a second primer wherein 5' sequence of said first primer is complementary to 5' of one strand of the double stranded DNA (ie., a first linker) and the 5' sequence of said second primer is complementary to 5' of another strand of the double stranded DNA (ie., a second linker) so that whole length of the double stranded DNA is amplified. One having ordinary skill in the art at the time the invention was made would have been a reasonable

expectation of success to amplify a double stranded DNA using a first and a second primer wherein 5' sequence of said first primer is complementary to 5' of one strand of the double stranded DNA (ie., a first linker) and the 5' sequence of said second primer is complementary to 5' of another strand of the double stranded DNA (ie., a second linker).

Conclusion

12. Claims 3, 4, 20, 21, 23-29, 36-76, 85, and 86 are allowable if applicant adds a method step that adds a first linker sequence and a second linker sequence to the ends of a DNA molecule before step a) of claim 20.

13. No claim is allowed.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
January 24, 2005

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600